

REMARKS

The Examiner objected to claim 1 as being indefinite on the grounds that the expression “combining a quantity of one of a reducing sugar and a reducing polysaccharide” is unclear. Applicant has amended claim 1 to recite “a reducing sugar”. It is submitted that a person skilled in the art would readily understand that a reducing sugar encompasses a reducing polysaccharide.

Applicant has amended claim to include a semi-colon after the first occurrence of the term “solution”, as suggested by the Examiner. In addition, applicant has amended claim 2 to employ Markush language, as suggested by the Examiner.

The Examiner has objected to the claims as being obvious in view of the cited references. Applicant respectfully submits that this objection should be withdrawn in view of the following remarks.

The claimed invention is a method of glycating a protein. The method involves the steps of combining a quantity of a reducing sugar with the protein in a solution; lyophilizing the solution to produce a lyophilized sample; placing the lyophilized sample under vacuum; and heating the lyophilized sample under vacuum.

The cited references disclose glycation methods that are not carried out under vacuum. In addition, Tarelli discloses a method that does not even involve glycating protein.

The claimed invention solves several deficiencies of the glycation methods disclosed by the cited references. The major deficiencies of the methods disclosed by the cited references that are solved by the instant invention are as follows: 1) incomplete glycation, i.e. the extent of glycation is low; 2) heterogeneous glycation products are obtained by the methods disclosed by the cited references; 3) advanced glycation end products (AGEs) are obtained on heating during the glycation procedure; 4) the glycation process is water slow and takes several days to achieve a measurable extent of glycation; and 5) the glycation products are unstable.

All of these limitations and difficulties with the prior art glycation processes are solved by lyophilization of a solution of protein and reducing sugar following by subjecting this lyophilized mixture to a vacuum and heating.

Carrying out the glycation under vacuum at elevated temperatures gives the following advantageous features that were not achieved by the methods of the cited references:

- 1) Complete glycation is achieved.
- 2) A homogeneous glycation product is obtained.
- 3) The product is chemically characterized as a ketoamine.
- 4) No advanced glycation end products are obtained.

The inventive feature of the instant invention is that the glycation is carried out under vacuum. In a vacuum, no oxygen is present which prevents the formation of advanced glycation end products. Also, the vacuum promotes the condensation reaction so that complete glycation is achieved thus yielded a homogeneous glycation product. This is a unique and unexpected result that is not suggested by any of the cited references either alone or in combination.

From the three cited references, it is not obvious to one skilled in the art that carrying out the glycation in vacuo would yield a homogeneous ketoamine glycation product. Tarrelli et al. in citation 3, state "This (glycation) adduct may be cyclic, a five-membered acetal ring by analogy with the acetone adduct, or may exist as a glycosyl amine; however it is not possible to determine form the results which is the case." In citation 2, Boratynski states "The chemistry of the reaction is not clear at present, although we would like to speculate that the dry thermal glycation might follow a general mechanism of non-enzymatic glycosylation"

Therefore it is not obvious to one skilled in the art that carrying out the glycation under a vacuum would eliminate the problems and deficiencies in the current glycation methodologies used for the glycation of proteins and yield a homogeneous ketoamine product.

It is therefore respectfully submitted that the claimed invention patentably distinguishes over the cited references.

As requested by the Examiner, applicant encloses a copy of the Tarelli et al. reference, "Lysine vasopressin undergoes rapid glycation in the presence of reducing sugars", Journal of Pharmaceutical & Biomedical Analysis, Vol. 12, No. 11, pp. 1355-1361, 1994.

Favourable consideration and allowance of this application are respectfully requested.

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